Preface

In the past decade there has been a growing public interest and resurgence in research in the field of hormonal carcinogenesis. This is due to the widespread use of therapeutic hormonal agents worldwide and to the increasing awareness of the causal association of hormones, both endogenous and exogenously administered, and a variety of human cancers. These associations include estrogens in uterine, cervical, vaginal, liver, testicular, prostatic, and possible breast cancers; progesterone and progestational hormones in breast cancer; androgens and anabolic steroids in hepatic and prostatic cancers. Additionally, gonadotrophins play a role in the etiology of ovarian and testicular cancers and thyroid-stimulating hormones in thyroid cancers. Therefore, hormonal carcinogenesis encompasses the study of both natural and synthetic hormonal agents, including growth factors and other peptide and protein factors, which contribute substantially to the *etiology* of both human and animal neoplasms, benign or malignant. Hormones may be involved in all aspects of neoplastic transformation, including initiation, promotion, and progression, and the inhibition of these processes.

There are a number of important issues in women's health that need to be addressed. More than 40 million U.S. women are menopausal, and these women have a life expectancy of over 30 years after the menopause. When these figures are multiplied worldwide, the numbers become staggering. After the menopause, estrogen replacement therapy (ERT) is the choice of most women in industrialized countries. Still unresolved is whether or not concomitant progestational hormone treatment, now commonly given with ERT, will increase the risk for breast cancer in women.

The benefits of ERT for hot flashes, osteoporosis, cardiovascular disease, genitourinary dysfunction, nervous, psychological, and sexual functions are well established. Recently, the beneficial use of estrogens in relation to heart disease has been publicized in a Boston study. While there is concern regarding the widespread and recent rise in the use of oral contraceptives (OCs), among OC users there is evidence for a significant reduction in the incidence of benign breast disease, ovarian cysts, iron deficiency anemia, pelvic inflammatory disease, and ectopic pregnancy.

Despite the evident and substantial benefits derived from these hormonal agents, safer preparations appear mandatory in light of their carcinogenic

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potential. It is also essential that we have a greater understanding of the normal physiologic, biochemical, and molecular processes by which hormones affect cell proliferation, differentiation, and ultimately, neoplastic processes. Many fundamental questions remain unresolved. Although it seems clear that hormones can result in tumor promotion by virtue of their ability to affect cell proliferation and differentiation, there is as yet no concensus on whether or not hormones can act as nongenotoxic or genotoxic carcinogens. Even in the absence of other chemical or physical agents, it is not known whether hormone-induced tumor formation is a result of some intrinsic property of the parent hormone molecule operating through a specific receptor mechanism, or whether a metabolite(s) interacts directly with the genetic apparatus of target cells. It is also not known whether such events bring about specific chromosomal alterations or abnormalities, mutations, translocations, or permanent gene reiterations that would lead to hormonally induced neoplastic transformation.

Because of the high relative human risk, understanding the endocrine involvement in the etiology of breast and prostate cancer should be given a high priority. There is no agreement, for example, whether or not ERT should be given to women who have been previously treated for breast cancer or other endocrine-associated malignancies. A related issue of equal urgency is determining whether DES daughters and their progeny are at higher risk for endocrine-related neoplasms.

In an effort to respond to the growing interest in hormonal carcinogenesis, and to address these timely questions, the First International Symposium on Hormonal Carcinogenesis was convened in Cancun, Mexico. This symposium brought together scientists from a wide variety of disciplines. They included clinicians, epidemiologists, pathologists, endocrinologists, reproductive toxicologists, cell and molecular biologists, biochemists, pharmacologists, and chemists, who presented and discussed their individual approaches and identified fruitful lines of research to elucidate the involvement of hormones in neoplastic processes.

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